In the Specification

Please replace the paragraph beginning on page 7, line 22 with the following rewritten paragraph:

B1

Figure 8, panel A, depicts the timecourse of the experiment on tumor growth and metastasis in tumor-bearing mice. Figure 8, panel B, is a graph depicting tumor volume in mice treated with PBS, inactive heparinase III, active heparinase III, ~~as well as mice treated with~~ and heparinase I.

Please replace the paragraph beginning on page 8, line 8 with the following rewritten paragraph:

B2

Figure 13, panel A, depicts the ~~results of compositional analysis of HLGAG saccharide fragments released from B16BL6 cells.~~analysis of the heparinase I-generated fragments. Figure 13, panel B, depicts the analysis of the heparinase III-generated fragments. Figure 13, panel C, depicts the analysis with PBS as a control. Figure 13, panel D, provides a table showing the relative percentage of HLGAG disaccharides in the heparinase I and heparinase III-generated fragments. Figure 13, panels E and F, show the mass spectrometric oligosaccharide mapping of heparinase I and heparinase III derived HLGAG saccharide fragments.

Please replace the paragraph beginning on page 64, line 10 with the following rewritten paragraph:

B3

a. ***Methods:*** B16BL6 cells in 10 cm culture dishes were serum starved for 48 hours before stimulation with 50 ng/ml FGF2. Cells were stimulated for 20 minutes before whole cell lysates were prepared with 1 ml modified RIPA buffer containing various enzyme inhibitors (50 mM Tris-HCl, pH 7.4, 1% NP-40, 0.25% Na-deoxycholate, 150 mM NaCl, 1 mM EDTA, 1 mM PMSF, 1 μg/ml aprotinin, leupeptin, and pepstatin, 1 mM activated Na_3VO_4, 1 mM NaF). Protein concentration in the lysate was determined using the Bio-Rad protein assay kit (BioRad) and adjusted accordingly for electrophoresis analysis. For the heparinase treated groups, cells were treated with either hep I or hep III (200 nM) for 30 min at 37 ^{0}C prior to addition of FGF2.

The immunoblot was probed with anti-Erk-1, 2 or anti-phospho-Erk-1, 2 antibody (New England Biolabs; MA) and detected by anti-rabbit IgG conjugated to HRP using SuperSignal West Pico Chemiluminescent substrate (Pierce, IL).

Please replace the paragraph beginning on page 67, line 8 with the following rewritten paragraph:

Methods: ~~**a-c,**~~ Assessment of FGF2 signaling *in vivo* with the rat corneal pocket assay. Representative slit lamp photographs of rat corneas on day 6 after implantation with Hydron pellets containing FGF2, hep I fragments with FGF2, and hep III fragments with FGF2. The amount of FGF2 loaded into each pellet was ~120 ng, and the amount of HLGAG fragments was approximately 1 ng. The pellets were prepared and implanted essentially as described (Kenyon, B. M. *et al.* A model of angiogenesis in the mouse cornea. *Invest Ophthalmol Vis Sci* **37**, 1625-32 (1996)). On day 6 after the implantation into the cornea of Sprague-Dawley rats (n=5), the corneal neovascularization was photographed with a slit lamp and the extent of neovascularization was expressed as linear length and circumferential clock hours as described (Kenyon, B. M. *et al.* A model of angiogenesis in the mouse cornea. *Invest Ophthalmol Vis Sci* **37**, 1625-32 (1996)). Results are summarized in the table. Control pellets containing no FGF2 failed to induce neovascularization. It was noted that the inhibition of neovascularization by hep III derived fragments are dose dependent, with initial inhibition observed at about 0.02 ng/pellet. In addition, the inhibition of neovascularization by hep III derived fragments was found to be independent of the site of implantation, with similar inhibition observed when hep III derived fragments was implanted as a second pellet in between the FGF2 only pellet and the limbus. # Indicates mean and SE.

B4

Please replace the paragraph beginning on page 67, line 26 with the following rewritten paragraph:

B5

~~**b,**~~ *Model of the formation of cryptic HLGAG modulators of FGF2 signaling.* Interaction of HLGAGs (as part of proteoglycans) with the heparin-binding domains of FGF2 and FGFR

allows the formation of a ternary complex at the cell surface that forms the basis of FGF2 signaling. Digestion of the cell HLGAG coat with hep I releases fragments with an appropriate spatial display of 2 O-, 6 O- and N-sulfated groups that would allow an optimal "fit" to both FGF2 and FGFR, leading to signaling through tyrosine kinase activation. Conversely, hep III-generated HLGAG fragments display another pattern of sulfated groups are still able to bind FGF2 but fail to form a constructive signaling complex at the cell surface, thus inhibiting FGF2 activity.